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SYNTHESIS AND ANTIMICROBIAL EVALUATION OF SOME NOVEL HETEROCYCLIC COMPOUNDS

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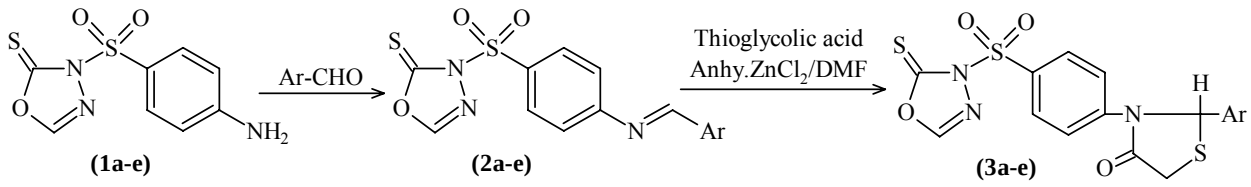
ABSTRACT

3-(4-Aminophenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione **(1)** undergoes facile condensation with aromatic aldehydes to afford the corresponding 3-(4-(substituted benzylideneamino)phenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thiones **(2a-e)** in good yields. Cyclocondensation of compounds **(2a-e)** with thioglycolic acid yields 2-subsituted phenyl-3-(4-(2-thioxo-1,3,4-oxadiazol-3(2H)-ylsulfonyl) phenyl) thiazolidin-4-ones **(3a-e)**. The structures of these compounds were established on the basis of analytical and spectral data. All the newly synthesized compounds were evaluated for their antibacterial and antifungal activities.

Key words: 3-(4-Aminophenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione, Schiff base thiazolidine, Antibacterial activity.

INTRODUCTION

The heterocyclic compounds such as, 4-thiazolidinones[1,2], fused thiazolidinones[3,4], 2-pyrrole and 2-pyrrolidinones[4,5], 1,3,5-oxadiazine[1] and tetrazole[6] have prominent role in pharmaceutical drugs. Literature assessment reveals that Schiff bases indicate that they have coordinating behaviors with the transition metal ions. Schiff bases also display biochemical and physiochemical effects[7-10]. The another moiety dihydrothieno[3,2-c]pyridine also have pharmaceutical activity[11-13]. If both these moiety are clubbed into one molecule, it will be a good bioactive compound. 4-Thiazolidinones are also known to exhibit antitubercular[14], antibacterial[15], antifungal[16] and anticonvulsant activities. Hence, it was thought of interest to merge both the thiazolidinone and 3-(4-aminophenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione moieties, which may enhance the drug activity of compounds to some extent or they might possess some of the above mentioned biological activities. Hence, the present communication comprises the synthesis of 2-subsituted phenyl-3-(4-(2-thioxo-1,3,4-oxadiazol-3(2H)-ylsulfonyl) phenyl) thiazolidin-4-ones **(3a-e)**. The synthetic approach is shown in **Scheme 1**.



Where Ar = (a) C_6H_5, (b) 2-OH-C_6H_4, (c) 4-OH-C_6H_4, (d) 4-OCH_3-C_6H_4 (e) 4-Cl-C_6H_4

Scheme 1

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EXPERIMENTAL

Materials

All chemicals used were of laboratory grade. 3-(4-Aminophenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione was prepared by reported method[17].

Measurement

Melting points were determined in open capillary tubes and are uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively.

Preparation of 3-(4-(substituted benzylideneamino)phenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thiones (2a-e): A mixture of 3-(4-aminophenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione **(1)**, (0.01 mole) and the aromatic aldehydes **(a-e)** in ethanol (15 mL) was refluxed on a water bath for 2-3 hrs. The solid separated was collected by filtration, dried and recrystallized from ethanol. The yields, melting points and other characterization data of these compounds are given in Table 1.

Preparation 2-subsituted phenyl-3-(4-(2-thioxo-1,3,4-oxadiazol-3(2H)-ylsulfonyl) phenyl) thiazolidin-4-one (3a-e): A mixture 3-(4-(substituted benzylideneamino)phenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione **(2a-e)** (0.01 mole) in THF (30 mL) and mercaptoacetic acid (thioglycolic acid) (0.01 mole) with a pinch of anhydrous $ZnCl_2$ was refluxed for 13-14 hrs. The solvent was then removed to get a residue, which was dissolved in benzene and passed through a column of silica gel using benzene: chloroform (7.5 : 2.5; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 2-subsituted phenyl-3-(4-(2-thioxo-1,3,4-oxadiazol-3(2H)-ylsulfonyl) phenyl) thiazolidin-4-ones **(3a-e)**, which were obtained in good yield. The yields, melting points and other characterization data of these compounds are given in Table 2.

Table 1: Analytical data and elemental analysis of compounds (2a-e)

Comp.	Molecular formula (Mol. wt.)	Yield (%)	M.P.* (°C)	Elemental analysis							
				% C		% H		% N		% S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
2a	$C_{15}H_{11}N_3O_3S_2$ (345)	79	212-214	52.14	52.16	3.20	3.21	12.14	12.17	18.54	18.57
2b	$C_{15}H_{11}N_3O_4S_2$ (361)	76	223-224	49.83	49.85	3.05	3.07	11.60	11.63	17.70	17.75
2c	$C_{15}H_{11}N_3O_4S_2$ (361)	78	217-219	49.82	49.85	3.06	3.07	11.62	11.63	17.72	17.75
2d	$C_{16}H_{13}N_3O_4S_2$ (375)	75	202-203	51.17	51.19	3.46	3.49	11.16	11.19	17.04	17.08
2e	$C_{15}H_{10}N_3O_3S_2Cl$ (378.5)	76	214-216	47.42	47.43	2.62	2.65	11.04	11.06	16.86	16.88

*Uncorrected

Table 2: Analytical data and elemental analysis of compounds (3a-e)

Comp.	Molecular formula (Mol. wt.)	Yield (%)	M.P.* (^{0}C)	Elemental analysis							
				%C		%H		%N		%S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
3a	$C_{17}H_{13}N_3O_4S_3$ (419)	71	223-225	48.65	48.67	3.11	3.12	10.00	10.02	22.92	22.93
3b	$C_{17}H_{13}N_3O_5S_3$ (435)	68	217-219	46.86	46.88	2.99	3.01	9.63	9.65	22.07	22.09
3c	$C_{17}H_{13}N_3O_5S_3$ (435)	66	208-210	46.87	46.88	3.00	3.01	9.62	9.65	22.06	22.09
3d	$C_{18}H_{15}N_3O_5S_3$ (449)	67	212-214	48.06	48.09	3.34	3.36	9.33	9.35	21.38	21.40
3e	$C_{17}H_{12}N_3O_4S_3Cl$ (452.5)	69	216-218	44.97	44.98	2.64	2.66	9.24	9.26	21.16	21.19

*****Uncorrected

Biological screening

Antibacterial activities

The antibacterial activities of all the compounds were studied against gram-positive bacteria (*Staphylococcus aureus and Bacillus subtilis*) and gram-negative bacteria (*E. coli, and Klebsiella promioe*) at a concentration of 50 µg/mL by agar cup plate method. Methanol system was used as control in this method. Tetracycline was used as a standard for comparison. The area of inhibition of zone was measured (mm). Compounds **(3e)** and **(3d)** were found more toxic for microbes. Other compounds were found less or moderate active than tetracycline (Tables 3).

Table 3: Antibacterial activity of compounds (3a-e)

Compounds	Gram +ve		Gram -ve	
	Staphylococcus aureus	***Bacillus subtilis***	***E. coli***	***Klebsiella promioe***
3a	46	63	62	67
3b	47	64	62	69
3c	49	68	65	73
3d	53	74	72	80
3e	51	72	69	77
Tetracycline	55	79	74	84

Antifungal activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration *in vitro*. Plant pathogenic organisms *Nigrospora Sp, Aspergillus niger, Botrydepladia thiobromine, and Rhizopus nigricum*

were used. The antifungal activities of all the compounds **(3a-e)** were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato (200 g), dextrose (20 g), agar (20 g) and water (1 mL). Five days old cultures were employed. The compounds to be tested were suspended (1000 ppm) in a PDA medium and autoclaved at 120^{o}C for 15 min. at 15 atm. pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula –

$$\text{Percentage of inhibition} = 100\ (X-Y) / X$$

Where, X = Area of colony in control plate and

Y = Area of colony in test plate

The fungicidal activity displayed by various compounds **(3a-e)** is shown in Tables 4.

Table 4: Antifungal activity of compounds (3a-e)

Compounds	*Nigrospora Sp.*	*Aspergillus Niger*	*Botrydepladia Thiobromine*	*Rhizopus Nigricum*
3a	59	51	62	56
3b	61	53	62	60
3c	67	65	63	58
3d	73	68	73	64
3e	70	72	69	62

RESULTS AND DISCUSSION

It was observed that 3-(4-aminophenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thione **(1)** undergoes facile condensation with aromatic aldehydes to afford the corresponding 3-(4-(substituted benzylideneamino) phenylsulfonyl)-1,3,4-oxadiazole-2(3H)-thiones **(2a-e)**. The structures of **(2a-e)** were confirmed by elemental analysis and IR spectra showing absorption bands at 1630-1670 cm^{-1} (C=N), 3030-3080 cm^{-1} (C-H, of Ar.) and 2815-2850 cm^{-1} (-OCH_3). ^{1}H NMR: 7.52-7.86 (8 H, m) (Ar - H), 8.43-8.80 (1 H, s) (-N=CH), 7.52-7.56 (1H, s) (oxadiazole ring N=CH), 2d; 3.90 (3H, s) (-OCH_3). ^{13}C NMR: 155.6-122.8 (Ar-12C), 190.4(-CS), 150.8 (oxadiazole ring), 160.3 (-N=CH); 2b: 55.5-56.7 (-OCH_3). The C, H and N analysis data of all compounds are presented in Table 1.

The structures assigned to 2-subsituted phenyl-3-(4-(2-thioxo-1,3,4-oxadiazol-3(2H)-ylsulfonyl) phenyl) thiazolidin-4-ones **(3a-e)** were supported by the elemental analysis and IR spectra showing absorption bands at 1690 cm^{-1} (C=O of thiazolidinone ring), 718 cm^{-1} (C-S-C of thiazolidinone ring), 3075-3095 cm^{-1} (CH_2 of thiazolidinone ring) and 3030-3080 cm^{-1} (C-H, of Ar.). ^{1}H NMR: 7.92-7.28 (8H, m) (Ar - H), 6.50 (1H, s) (CH), 4.2-3.8 (2H, s) (thiazole ring -CH), 7.52-7.56 (1H, s) (oxadiazole ring N=CH), 3d; 3.90 (3H, s) (-OCH_3). ^{13}C NMR: 122.2-145.4 (Ar-12C), 171.6 (-CO), 189.8 (-CS), 150.8 (oxadiazole ring), 72.6 (CH), 34.2 (CH_2), 3d: 55.5-56.7 (-OCH_3). The C, H, N and S analysis data of all compounds are presented in Table 2.

The examination of elemental analytical data reveals that the elemental contents are consistent with the predicted structure shown in **Scheme 1**. The IR data also support the assignment of the predicted structure.

REFERENCES

1. C. M. Da Silva, D. L. Da Silva and L. V. Modolo, J. Adv. Res., **2**, 1 (2011).
2. Refat El-Sayed, Indian J. Chem., **45(B)**, 738 (2006).
3. S. Fustero, A. Simon-Fuentes and J. F. Sanz-Cervera, Org. Prep. Proced. Int., **41**, 253 (2009).
4. J. Kothari, M. A. Mehloff, S. P. Singh, S. S. Parmar and V. I. Stenderg, J. Heterocyclic Chem., **17**, 1393 (1980).
5. A. K. Sengupta and H. K. Misra, J. Indian Chem. Soc., **58**, 508 (1981).
6. H. L. Yale and J. J. Piala, J. Med. Chem., **9**, 42 (1966).
7. S. K. Singh and S. B. Singh, Indian J. Chem., **40**, 1070 (2001).
8. R. K. Agarwal, L. Singh and D. K. Sharma, Bioinorg. Chem. Appl., Article ID 59509 (2006).
9. V. K. Sharma, S. Srivastava and A. Srivastava, Bioinorg. Chem. Appl., Article ID 68374 (2007).
10. E. Labisbal, K. D. Haslow, A. Sousa-Perdrares, J. Valdes-Martinez, L. Hernandez-Ortega and D. X. West, Polyhedron, **22**, 2831 (2003).
11. L. Q. Al- Mawsawi, R. Dayam, L. Taheri, M. Witvrouw, Z. Debyser and N. Neamati, Bioorg. Med. Chem. Lett., **17(23)**, 6472 (2007).
12. C. Plasencia, R. Daym, Q. Wang, J. Pinski, T. R. Jr. Burke, D. I. Quinn and N. Neamati, Mol. Cancer Ther., **4(7)**, 1105 (2005).
13. H. Zhao, N. Neamati, S. Sunder, H. Hong, S. Wang, G. W. Milne, Y. Pommier and T. R. Jr. Burke, J. Med. Chem., **40(6)**, 937 (1997).
14. K. M. Mistry and K. R. Desai, E-J. Chem., **1(4)**, 189 (2004).
15. H. S. Patel and H. J. Mistry, Phosphorous, Sulfur and Silicon, **79**, 1085 (2004).
16. J. J. Bhatt, B. R. Shah and N. C. Desai, Indian J. Chem., **33B**, 189 (1994).
17. Z. Turgut, C. Yolacan, F. Aydogan and N. Ocal, Molecules, **12**, 2151 (2007).